Accordingly, the obviousness-type double patenting rejection should be held in abeyance until a final set of allowed claims is found in both applications. Once Applicants have determined which claims are allowable, Applicants will be able to determine if a Terminal Disclaimer is appropriate.

Claims 1-12 were rejected for obviousness-type double patenting as being unpatentable over claims 29, 30 and 33-35 of co-pending application Serial No. 07/919,297. As with the rejection over Serial No. 08/031,801, this obviousness-type double patenting rejection is only a provisional rejection. Accordingly, Applicants request that this rejection be held in abeyance until otherwise allowable claims are found in both applications.

**Finality of Rejection**

Applicants wish to thank the Examiner for reconsidering the application and withdrawing the finality of the rejection mailed March 29, 1995.

**35 U.S.C. § 103**

I. **Rejection Over Huxley, Hooper and Pachnis.**

Claims 1-6, 8 and 9 were rejected under 35 U.S.C. § 103 as being obvious over Huxley taken with Hooper and Pachnis.

**The References Do Not Provide A Reasonable Expectation Of Success**

The rejection is respectfully traversed. A rejection of claims under 35 U.S.C. § 103 as being obvious to try requires both a suggestion of the invention and a reasonable

expectation of success, see In re O'Farrell 7 USPQ2d 1673 (Fed. Cir. 1988). As discussed in the response filed July 31, 1995, Applicants maintain that the publications cited by the office do not provide a reasonable expectation of success in producing the claimed invention. Absent a showing of a reasonable expectation of success, a *prima facie* case of obviousness cannot be established.

Applicants respectfully submit that the Office's rejection has failed to establish a reasonable expectation of success for the claimed invention. The Office's arguments are drawn to an improper "not impossible" standard rather than the "reasonable expectation of success" standard required for establishing a prima facie case of obviousness. The Office has argued that the prior art does not teach that a yeast spheroplast cannot be fused to an ES cell so as to introduce a YAC into an ES cell. The Office maintains that Strauss (Science), Strauss (EMBO), and Bradley do not teach away from the claimed invention because they do not teach that a yeast spheroplast cannot fuse to an ES cell. In effect, the Office has argued that because the art does not teach that spheroplast fusion is impossible, there is a reasonable expectation of success. In making its arguments in this manner, the Office has ignored the question of whether there was a reasonable expectation of producing YAC containing ES cells that may be successfully transferred to blastocyst and proceed through embryonic development so that a xenogeneic segment on the YAC becomes integrated into the germline cells of the resultant chimeric animals. Claims 2-12 explicitly recite this limitation about integration of the xenogeneic DNA

segment into the germline. Furthermore, even though claim 1 does not contain any express limitation about the presence of a xenogeneic DNA segment in germline cells, the method of Claim 1 has an unexpected advantage. This unexpected advantage is that the xenogeneic DNA segment containing ES cells produced by the method of Claim 1 may be transferred to a blastocyst, wherein the xenogeneic DNA segment is incorporated into the germline of the resultant animal.

In the responses previously filed by Applicants, several publications have been provided to show that yeast spheroplast fusion with ES cells has a low probability of producing genetically modified ES cells that can be successfully incorporated into a developing embryo. These publications include Strauss (Science), Strauss (EMBO), and Bradley. These publications teach that the large amount of yeast chromosomal DNA introduced through yeast spheroplast fusion would be likely to interfere with the ability of ES cells to properly differentiate during embryogenesis, thereby preventing transgenes from being incorporated into the germlines of chimeric animals. Accordingly, Strauss (Science), Strauss (EMBO), and Bradley teach away from the claimed invention.

**The Office has granted undue weight to a speculative statement in Pachnis**

The Office has stated that it does not consider the Applicants' arguments in the response filed July 31, 1995 to be persuasive. With respect to the Pachnis publication, the Office has stated that Pachnis provides a reasonable expectation of success for introducing YACs into ES cells

using yeast spheroplasts because Pachnis contains a sentence indicating that such an experiment should be attempted. Pachnis does not provide a description of methods for performing these experiments or describe experiments in which ES cells have been modified.

It is the Office's position that this one speculative statement in Pachnis provides a reasonable expectation of success in fusing YAC-containing yeast spheroplasts to embryonic stem cells so as to provide a method of modifying the genome of the embryonic stem cell. Contrary to the Office's position, Pachnis does not provide a reasonable set expectation of success, instead, Pachnis at most, provides an invitation to future experimentation. The Office has taken this invitation for future experimentation as irrebuttable proof that Pachnis provides a reasonable expectation of success. The Office's reliance on Pachnis is misplaced. The fact that Pachnis may suggest an experiment, does not prove that the Pachnis publication provides a reasonable expectation of success. It is well established in case law that an "obviousness-to-try" standard is not a sufficient basis for rendering an invention obvious under 35 U.S.C. § 103. This point is clearly set forth in In re Eli Lilly & Co. 14 USPQ2d 1741 (Fed. Cir. 1990) where the Court held:

> "An obvious to try" situation exists when a general disclosure may pique the scientists curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, **or that the claimed result will be obtained** if certain directions were pursued. (Emphasis Added)

If, as the Office assumes, a publication's suggestion that an experiment be tried is dispositive of the issue of whether or not there is a reasonable expectation of success, the position of the Federal Circuit on the obvious-to-try standard would be rendered meaningless.

**The Claims recite a yeast spheroplast mediated transformation step**

The Office has noted that Applicants have argued that Pachnis does not state that L cells and ES cells are equivalent to one another and provides no guidance for transforming ES cells. The Office believes this argument is irrelevant because the claims are not drawn to methods for transforming ES cells. Applicants respectfully disagree. The claimed methods recite a fusion step resulting in the transformation of ES cells. If such a step is not obvious over the prior art, then the claims cannot be obvious over the prior art.

Furthermore, the Office has not shown why L and ES cells should be considered equivalent to one another. It is common knowledge that L cells are terminally differentiated, whereas ES cells remain totipotent. Any modification of ES cells that would interfere with the totipotency of the ES cells would render the ES cells effectively useless for generating transgenic animals. Clearly, L cells and ES cells are not functionally equivalent to each other.

**Yeast spheroplast fusion necessarily introduces yeast chromosomal DNA into transfectants**

Applicants have cited Strauss (Science) as evidence that the Pachnis technique would not be expected to work with ES cells. The Office maintains that Strauss (Science) does not contain a teaching that problems exist with the use of spheroplast fusions, and, specifically, that the paragraph on page 421, right hand column of Strauss, does not provide support for the Applicants' position. Strauss (EMBO) at page 421, right column, third full paragraph, indicates that the presence of a large portion of the yeast genome present as contaminants:

> "could be mutagenic, and thus deleterious to the capacity of an ES cell to contribute to the germ line of a chimeric mouse."

The Office has stated that this paragraph does not contain "a single teaching that there is a problem in the use of spheroplasts per se." Applicants respectfully disagree with the Office's analysis of Strauss (EMBO). Strauss (EMBO) describes the introduction of purified YACs into L cells by lipid micelles as a desirable alternative to yeast spheroplast fusion. Yeast spheroplast fusion and related techniques in which the entire yeast genome is introduced into a mammalian cell are considered undesirable because of the mutagenesis that may occur as a result of introduction of a large amount of undesirable yeast DNA that may randomly insert into the mammalian chromosome.

Strauss (EMBO) discloses that the YACs constitute such a small fraction of the DNA available for transfection that a large portion of the stable transfectants contained portions

of the yeast genome. The Office has asserted that Strauss (EMBO) was not able to achieve transection of ES cells because a large amount of DNA in the spheroplast consists of the yeast genome and not the YAC of interest. The Office postulates that the inability to achieve transection is not related to this spheroplast technique per se but to the relative ratios of the junk DNA compared to the desired DNA. **However, the Office's argument that there is no problem with the spheroplast technique per se is unsupported and scientifically baseless. There is no way to disassociate the effects of introducing a high level of "junk" DNA from the use of yeast spheroplast fusions because yeast spheroplasts necessarily comprise "junk" DNA.**

YAC containing yeast spheroplasts, in addition to containing the desired YAC, necessarily contain the yeast genome ("junk" DNA). Applicants are unaware of any method of producing a YAC-containing yeast spheroplast for fusion that is devoid of the yeast genome. Thus, the distinction the Office makes between problems with yeast spheroplast fusion per se and the high "junk" DNA to YAC DNA ratio problem is irrelevant because these effects cannot be separated.

Strauss (EMBO) clearly recognizes this problem (as can be seen in the citation from page 421) and seeks to avoid it by introducing purified YAC DNA into mammalian cells without the "junk" DNA introduction problem inherent in the spheroplast fusion technique. Thus, Strauss (EMBO) teaches away from the use of yeast spheroplast fusion and demonstrates the absence of a reasonable expectation of success. Moreover, Strauss (EMBO) and Strauss (Science) acknowledge that this problem

with "junk" DNA is of particular significance for ES cells. As noted above, ES cells must retain their totipotency after genetic manipulation so that the manipulated cells may be introduced into a blastocyst and subsequently become a pact of a chimeric animal. Introducing a large amount of unwanted and uncharacterized yeast genome DNA into an ES cell would be expected to have deleterious effect on ES and cell function. For example, the yeast genomic DNA could insertionally inactivate genes, insertionally activate genes, be expressed upon insertion, and the like. It was the Applicants who, contrary to the teachings of the art, demonstrated that viable ES cells containing YAC mediated xenogeneic DNA could be generated through yeast spheroplast fusion and successfully introduced into embryos.

**The Office's proposed solution to the problems described in the Strauss publications does not alter the fact that the publications teach away from the claimed invention**

While Strauss (EMBO) considers the problem of yeast genome contamination of ES cells transformed by yeast spheroplast fusion to be highly significant, the Office believes that no such problem exists. The Office maintains that this problem could be avoided by the suggested solution, i.e., screening a larger number of transfectants. The Office explains that this selection is possible because the identification of a clone containing the desired YAC DNA is "relatively straightforward" using techniques known to the person of ordinary skill in the art. Because the Office has proposed a solution to the problem stated in both Strauss (EMBO) and Strauss (Science), the Office contends that these

publications do not teach away from the use of the spheroplasts to modify ES cells.

**Applicants respectfully submit that the Office's analysis of the Strauss publications as not teaching away from the use of the spheroplast to transform ES cells is clearly wrong as a matter of law and as a matter of scientific fact.** Strauss (EMBO) contains explicit language (Page 1907, last paragraph, first column) stating they have developed a new technique for transforming mammalian cells with gel-purified YAC DNA so as to avoid the spheroplast fusion problems resulting from the introduction of yeast genomic DNA into ES cells.

The fact that the Office can speculate as to a solution that the Office believes might work is improper and irrelevant to an analysis of whether Strauss publications teach away from the claimed invention. A publication must be considered for what it teaches. The Federal Circuit in In re Gurley 31 USPQ2d 1130 (Fed. Cir. 1994) held:

> "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be in a direction divergent from the path that was taken by the Applicant."

As the Strauss publications teach that there are problems with the use of yeast spheroplast fusions with ES cells. The Strauss publications necessarily teach away from the claimed invention, irrespective of the Office's proposed solutions.

**The Office's proposed solution to the problems described in the Strauss publications cannot work**

**Applicants note that the Office's proposed solution to the problem of transforming ES cells with yeast spheroplasts as described in the Strauss publication is scientifically incorrect and not supported by any prior art publication.**

As noted in both Strauss publications and by the Office, yeast spheroplast containing YACs comprise (include) a much higher level (at least several orders of magnitude) of yeast genome DNA than YAC DNA. Each fusion between a yeast spheroplast and an ES cell should result in the **simultaneous** introduction of YAC DNA and a much larger amount of yeast genome DNA. Accordingly, one would expect an ES cell to be cotransfected with both YAC DNA and a much larger amount of yeast genome DNA during a spheroplast fusion. Screening a larger number of transfectants, as suggested by the Office, would not reveal ES cells that were transformed solely with YAC DNA, i.e., free of contaminating yeast genome DNA. ES cells containing YAC DNA and no yeast genomic DNA could not be found because no mechanism exists for separating the two types of DNA that simultaneously enter the ES cell during spheroplast fusion. Thus, by screening a larger number of transfectants, the problem described in the Strauss publications would not be avoided.

Applicants note that the Office has not provided any references or other objective support of its position that the problems proposed in the Strauss publication could readily be resolved by screening more transfectants.

**If the Examiner cannot find any prior art references to support her position, Applicants formally request that the Examiner submit a declaration under 37 CFR § 107(b) explaining her basis for the scientific facts alleged.**

**The Office ignores the very reasons that another transformation vehicle is used in the Strauss publications**

The Office has stated that the problems with the fibroblast fusion techniques described in Pachnis, as reported in Strauss (EMBO) and Strauss (Science) are not relevant because Strauss (Science) uses lipid micelles and lipid micelles are not identical to yeast spheroplasts. The Office maintains that Strauss (Science) never discloses that lipid micelles are used as an alternative technique to spheroplast fusion because spheroplast fusion does not work. The Office's analysis of Strauss (Science) is incorrect. **Strauss (Science) uses lipid micelles rather than yeast spheroplasts to avoid the problem with yeast junk DNA -- the micelles contain only YAC DNA.** The fact that Strauss (Science) teaches an improved method of using micelles does not alter the fact that Strauss (Science) teaches away from using spheroplasts to modify ES cells. Indeed, Strauss (Science) at page 1907, last paragraph, first column, states,

> "[O]ther methods of introducing YAC-sized DNA into mammalian cells have been used, including spheroplast fusion and microinjection (16-21), **but no successful transection of ES cells has been reported to date.** Spheroplast fusion introduces the whole yeast genome into the transfected cells because **DNA injected into mammalian cells is highly mutagenic,** it is possible that the presence of yeast DNA in the transfected ES cells interferes

> with their ability to contribute to the germ line. The use of gel-purified DNA in ES cell transfections is consequently advantageous. The transection of DNA-lipid micelles resulted in a large fraction of the drug-resistant clones carrying an intact transgene and did not interfere with the totipotency of the manipulated ES cells." (Emphasis Added)

Thus, the cited portion of Strauss (Science) clearly shows that the use of yeast spheroplasts containing YACs to manipulate ES cells is <u>not</u> desirable as viewed by those skilled in the art. Specifically Strauss (Science) states that the additional yeast genomic DNA **is** mutagenic and that the presence of this mutagenic DNA could interfere with the ability of transfected ES cells to contribute to the germ line in chimeric animals. Strauss (Science) states that the use of purified YACs in lipid micelles avoids this problem of potential interference with subsequent embryonic development. Whether Strauss (Science) was correct about the effects of yeast genomic DNA is irrelevant. **Thus, contrary to the Office's assertion, Strauss (Science) teaches that spheroplast fusion with ES cells has never been successful and that lipid micelles should be used instead.** This is clearly a teaching away from the claimed invention.

Furthermore, the Office has asserted that screening larger numbers of clones would also overcome the mutagenicity problem associated with yeast genomic DNA. As previously discussed, the Office's reliance on the screening of additional clones to avoid this problem has no basis in scientific fact and is not supported by any publication or other information cited by the Office, or available in the art.

**Strauss (Science) teaches that yeast chromosomal DNA is mutagenic irrespective of the manner in which it is introduced into a mammalian cell**

The Office has stated that Strauss (Science) only describes mutagenesis problems with "injected DNA" and not spheroplast-introduced DNA. Applicants submit that the Office's characterization of Strauss (Science) is improper. Strauss (Science) describes problems with yeast spheroplast fusion and microinjection to manipulate ES cells. These problems stem from the fact that these procedures introduce unwanted genomic yeast DNA, as well as the desired YAC DNA, into the transfected cells. Strauss (Science) uses lipid micelles to avoid this problem of introducing unwanted yeast genomic DNA. It would be apparent to any person of ordinary skill in the art that Strauss (Science) used the term "injected DNA" as a more convenient grammatical alternative to the cumbersome phrase "spheroplast fusion and microinjected DNA."

In both cases, DNA is introduced or injected into the cell. The fact that the yeast genomic DNA is injected into the cell rather than introduced through spheroplast fusion does not alter the effects, i.e., mutagenicity of the unwanted genomic yeast DNA. The point that Strauss (Science) is clearly trying to make is that the large amount of yeast genomic DNA introduced into the transfected cell is undesirable and likely to have adverse effect on the function of the ES cell.

The distinction made by the Office between injection and fusion is without merit and does not support a conclusion that

the mutagenesis problems described in Strauss do not apply to spheroplast fusion.

**The prior art teaches that yeast chromosomal DNA is mutagenic and teaches away from the unnecessary introduction of yeast chromosomal DNA**

The Office has questioned whether or not yeast genomic DNA is mutagenic. The Office has cited Strauss (EMBO) at page 421, second paragraph, which states:

> [T]his contaminating material **could be** mutagenic, and thus deleterious to the capacity of an ES cell to contribute to the germline of a chimeric mouse. (Emphasis Added)

The Office contends that Strauss (EMBO) merely states that the genomic DNA **could be** mutagenic, not that the DNA is mutagenic. Applicants respectfully disagree with the Office's analysis of Strauss (EMBO). Rather than fairly considering what Strauss would suggest to a person of ordinary skill in the art, the Office appears to be arguing semantics. Yeast spheroplast fusion is expected to introduce large amounts of yeast genomic DNA into the cell in addition to whatever YAC DNA vector is present in the spheroplast. As this yeast genomic DNA may insert into the chromosome of the mammalian cell, the yeast DNA is expected to be mutagenic. Strauss (EMBO) clearly uses the term "could" because although there is a high possibility of the DNA being mutagenic, there is a chance that in any given experiment, a clone may be recovered that does not actually contain yeast genome DNA that has been inserted in such a way as to produce a deleterious mutation. By way of analogy, consider a billboard containing a warning that "driving a car while blindfolded **could** result in an accident."

Of course, it might actually be possible to occasionally drive a car while blindfolded and not get into an accident. Nonetheless, such a billboard would clearly teach away from driving a car while blindfolded.

In rebuttal to the express teachings of Strauss (EMBO), the Office has stated that there is no evidence that yeast genomic material is mutagenic. The Office further states that if the yeast DNA were truly mutagenic in ES cells, then insertion of any yeast DNA by any method would result in high rates of mutagenicity. Applicants respectfully submit that the Office is misconstruing the word "mutagenic" as it is used in the Strauss publications. Strauss (EMBO) is referring to the mutagenic effects of yeast genomic DNA caused by insertions of the yeast DNA into the chromosomes of ES cells.

Numerous publications teach that yeast genomic DNA is mutagenic. In contrast to the Office's position, Pavan demonstrates that yeast genomic DNA is inserted randomly into the chromosome of mammalian cells during yeast spheroplast fusion experiments. As noted on page 4168 of Pavan, last paragraph,

> "Our results demonstrate an additional limitation to this approach, in that uptake of YAC DNA is accompanied by inclusion of the significant portion of the yeast genome in the host cell. Yeast segments are likely to be transcriptionally inert in most cases. However, some fortuitous homology recognizable to the mammalian transcription apparatus cannot be ruled out, and insertion of yeast genome segments adjacent to a mammalian promoter could lead to gene expression. More importantly, each event in which a segment of yeast DNA is inserted into the mouse genome is a potential insertion **mutation** which could be carried into the animal."

Thus, Pavan describes the mutagenic effects of yeast genomic DNA that is introduced through spheroplast fusions. While yeast chromosomal DNA is mutagenic in all mammalian cells, this problem with mutagenicity is particularly significant in ES cells because ES cells must be able to retain their totipotent properties in order to be useful. Not only must genetically modified ES retain their totipotent properties in order to remain useful, the ES cells must be able to be integrated into the germline of the resultant chimeric animal. Developmental processes are highly complex and delicate. The introduction of a large amount of yeast chromosomal DNA would be expected to interfere with the developmental process.

This problem of incorporation of yeast genomic DNA is described in many other publications. For example, Gnirke *et al.*, EMBO J. 10:1629-1634 (1991), (a copy of which is enclosed with this response), at page 1633, next to the last paragraph of the left column, states:

> In all cases that were analyzed, a substantial portion of the yeast genome was maintained in the fusion cell lines along with the YAC

Thus, Gnirke clearly teaches that yeast chromosomal DNA is inserted into mammalian cell chromosomes after spheroplast fusion. Accordingly, Gnirke teaches that yeast genomic DNA (as introduced through spheroplast fusion) is mutagenic in the same way that Strauss (EMBO) and Pavan teach that yeast genomic DNA is mutagenic.

**Bradley teaches away from the claimed invention**

In the amendment previously filed by Applicants, Applicants have cited Bradley to show that the available prior art gave no reasonable expectation of success in using YACs to genetically modify ES cells so as to permit the modified ES to be successfully used to produce transgenic mice containing the desired YAC. Specifically, Bradley, at page 537, states:

> Large genes which are currently identified in yeast artificial chromosomes (YAC) vectors could potentially be transferred to ES cells and the mouse germ line although it still remains technically very difficult to effect such a transfer (i.e., the potential transfer of large genes using YAC vectors) and it is **unknown** whether ES cells modified with YACs will be able to repopulate the germline of mice. (Emphasis added.)

The Office has responded by asserting that Bradley does not provide evidence that YACs would not be expected to work in ES cells and that the term "potentially" as used in Bradley is not equivalent to the term "would not be expected," i.e., is not impossible. The Office has stated that Pachnis, as opposed to Bradley, postulates the successful use of YAC transfer to ES cells.

Applicants respectfully disagree with the Office's analysis of Bradley. First, Bradley is being cited as evidence that there was no reasonable expectation of success for introducing YACs into ES cells so as to provide for transgenic mice with YACs in the germline. The fact that Bradley does not actually carry out such experiments does not mean that Bradley is not evidence of a lack of a reasonable expectation of success. Bradley explicitly states that the effect of YACs on the ability of ES cells to repopulate the

germline of mice is **unknown**. Furthermore, the Office has taken the word "potentially" completely out of context. Bradley states that YACs could be potentially transferred into ES cells. Bradley goes on to state that the effects of YACs on the properties of ES cells to colonize the germline are **unknown**. For some reason, the Office has found that the invitation to future experimentation in Pachnis is more persuasive than the uncertainty expressed in Bradley. As previously noted, Pachnis, although not going into explicit detail about potential problems with introducing YACs into ES, merely states that the experiments should be attempted, not that there was a reasonable likelihood of success.

**The Office has failed to weigh the cited publications against one another**

Applicants wish to express concern with the Office's disparate analysis of publications cited by the Office and publications cited by the Applicants. Speculative statements in references cited by the Office have been irrebuttably presumed to provide a showing of a reasonable expectation of success. In contrast, every publication cited by the Applicants to demonstrate that the prior art teaches away from the claimed invention has been found to be of little weight with respect to determining if a reasonable expectation of success exists. This result is unfair to Applicants. In determining what constitutes a reasonable expectation of success, the Office must analyze the prior art as a whole and not selectively. As noted by the Federal Circuit in In re Young, 18 USPQ2d 1089 (Fed. Cir. 1989):

> When prior art contains apparently conflicting references, the Board must weigh each reference for its power to suggest solutions to an artisan or ordinary skill. The Board must consider all disclosures of the prior art .... to the extent that the references... are in the analogous fields...and thus would have been considered by a person of ordinary skill in the field of the invention. The Board, in weighing the suggestive power of each reference must consider the degree to which one reference might accurately discredit another."

The Office has clearly failed to weigh the publications against each other.

II. **Hooper, in view of Huxley and Pachnis**

Claims 7, 10, and 11 were rejected under 35 USC § 103 as being obvious over Hooper taken with Huxley and Pachnis. The rejection is respectfully traversed. As this rejection is essentially the same as the rejection of Claim 1-6, 8, and 9 over Huxley, Hooper, and Pachnis, the rejection is traversed essentially for the same reasons that the rejection of Claims 1-6, 8, and 9 was traversed, i.e., a person of ordinary skill in the art would not have a reasonable expectation of success in introducing YACs into ES cells by yeast spheroplast fusion.

III. **Huxley, in view of Hooper, Pachnis, Traver, Shimizu, and Berman**

Claim 12 was rejected under 35 USC § 103 as being obvious over Huxley, Hooper, Pachnis, as applied to Claim 1-6, 8, and further in view of Traver et al, Shimizu et al, and Berman et al.

The rejection is respectfully traversed for the reasons of record. Neither Traver, Shimizu, nor Berman, alone or in

combination with Huxley, Hooper, and Pachnis remedy the failure of Huxley, Hooper and Pachnis to provide a reasonable expectation of success. Accordingly, the rejection is improper and should be withdrawn.

**SUMMARY**

In view of the above remarks, the subject application is believed to be in good and proper order for allowance. Early notification of this effect is solicited.

When considering the above remarks, the Examiner is respectfully requested to adhere to the spirit of MPEP §706, which states:

> When an application discloses patentable subject matter and it is apparent from the claims and the applicant's arguments that the claims are intended to be directed to such patentable subject matter, but the claims in their present form cannot be allowed, because defects in the form of an omission of a limitation, the examiner should not stop with a bare objection or rejection of the claims. The examiner's action should be constructive in nature and when possible offer a definite suggestion for correction.
>
> If the examiner is satisfied after the search has been completed that patentable subject matter has been disclosed and the record indicates that the applicant intends to claim such subject matter, he or she may note in the office action that certain aspects or features of the patentable invention have not been claimed and that if properly claimed such claims may be given favorable consideration.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (415) 854-3660. Applicants would also be willing to have a personal interview with the Examiner, if the Examiner

intends to maintain the rejections of record. It is believed that such an interview could respond to any further questions that the Examiner may have in connection with the application.

The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 16-1150 for any matter in connection with this response, including any fee for extension of time, which may be required.

Respectfully submitted,

PENNIE & EDMONDS

Dated: 1/16/96

Albert P. Halluin reg 34,248 for 25,227 (Reg. No.)

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